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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,295	KOSTENIS, EVI	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-170* is/are pending in the application.

4a) Of the above claim(s) *57-170* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/28/01, 11/05/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims1 to 170 are pending in the instant application.

2) Claims 57 to 170 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the correspondence of 31 October of 2003. The traversal is on the ground(s) that a search of the different inventions in a single application would pose no undue burden. This is not found persuasive because M.P.E.P. 803 states that:

> " For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant."

Serious burden was shown in the original requirement by the separate classification and separate status in the art of the different inventions. Applicant has provided neither a showing nor evidence to the contrary.

Applicant is advised that the policy of searching as many as ten **nucleotide** sequences in a single application was discontinued several years ago because the sequence data bases have grown exponentially since the implementation of that policy. As a consequence, the search of more than one distinct sequence in a single application has proven to be unduly burdensome.

Finally, Applicant's assertion that the products of inventions 57 to 112 are produced by the process of claims 1 to 56 is factually flawed. Claims 1 to 56 are drawn to an **analytical** process that produces no product, other than information.

The requirement is still deemed proper and is therefore made FINAL.

3) This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence listing has been provided which includes the amino acid sequences presented in paragraph 062 of the instant specification. Applicant is required to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. §1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. Further, M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings".

For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Double Patenting

4) Applicant is advised that should claims 3, 9, 17, 23, 31, 37, 45, and 51 be found allowable, claims 4, 10, 18, 24, 32, 38, 46 and 52 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5) Claims 1, 2, 13, 14, 29, 30, 41 and 42 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Conklin et al. publication (Mol. Pharm. 50:885-890, 1996, cited by Applicant). The assays described in Figures 3 and 4 of this reference met all of the limitations of the instant claims either explicitly or implicitly. For example, it is old and well known in the art that all vertebrate cells produce multiple endogenous G proteins. Therefore, the CHO cells of Conklin et al. inherently meet the "produces at least two G-proteins" limitation of the instant claims.

6) Claims 1, 2, 13 to16, 27 to 30, 41 to 44, 55 and 56 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Coward et al. publication (Anal. Biochem.270:242-248, 01Jun. 1999, cited by Applicant). .

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7) Claims 1 to 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Conklin et al. patent publication (WO 99/05177, 04 Feb. 1999, cited by Applicant) in view of the Conklin et al. publication (Mol. Pharm. 50:885-890, 1996, cited by Applicant). These claims encompass a process of identifying pharmaceutical compounds having an effect upon a G protein-coupled receptor by applying that compound to a cell expressing that receptor and either or both of the two chimeric G alpha subunits –6qi4 and –6qs5, and measuring the effects of that compound upon the intracellular calcium concentration of that cell. The Conklin et al. patent publication, in general, described a method of identifying pharmaceutical compounds by employing a cell expressing a G protein-coupled receptor and a modified G alpha q subunit which has been rendered "promiscuous" relative to its receptor selectivity by the deletion of the first six amino acid residues from a native G alpha q subunit (page 14 therein). The text beginning in the last paragraph on page 15 of the Conklin et al. patent publication expressly taught the advantages of combining such a mutation with an additional mutation in which at least the last four amino acids from the truncated G alpha q subunit are replaced with the "corresponding residues of α_{i2} to create $\alpha_{q/}\alpha_{i}$ chimeras that can mediate stimulation of phospholipase C by receptors otherwise coupled exclusively to α_{i} ". The text beginning in line 10 on page 16 of that reference further taught that the

"switching based on C-terminal alterations from α_q to α_s", as taught "by Conklin et al. (in Molecular Pharmacology 50:885-890, 1996)" "can also be employed in the context of the present invention". The switch referred to the Conklin et al. patent publication appears to be "the replacement of the five carboxyl-terminal amino acids of α_q with the α_s sequence" described in the abstract of that reference. In essence, the Conklin et al. patent publication expressly suggested a method of identifying G protein-coupled receptor agonists by employing the chimeric G alpha subunits –6qi4 and –6qs5, amongst others. The text beginning in line 28 on page 2 and line15 on page 3 therein expressly taught that measuring calcium mobilization in such a system was "readily amenable to high throughput screening techniques". This reference taught all of the elements of the claimed assay and provided express motivation to combine those elements into an assay encompassed by the instant claims.

Claims 3, 4, 9, 10, 17, 18, 23, 24, 31, 32, 37, 38, 45, 46, 51 and 52 are distinguished from the other claims because they require the presence of two chimeric G alpha subunits and specifically encompass the combination –6qi4 and –6qs5. Line 7 on page 2 of the Conklin et al. patent publication discloses that "[m]ore than half of GPCRs appear to couple to the heterotrimeric G proteins G_S or G_i in which the α subunit is α_s or α_i." Because this patent publication taught that the employment of –6qi4 produced a system useful in the screening of Gi coupled receptors and, when combined with the Conklin et al. publication, taught that –6qs5 was useful for screening Gs coupled receptors, an artisan of ordinary skill in the art of molecular biology would have found it prima facie obvious to have combined these two chimeric G alpha subunits into

a single cell to produce a system that would be useful in screening for agonists of "more than half" of the known G protein-coupled receptors.

8) The Wedegaertner et al. publication (J. Biol. Chem. 268 (33):25001-25008, 1993) is being made of record because it discusses the criticality of palmitoylation to the functioning of G alpha subunits. This reference discloses that the elimination of palmitoylation from a G alpha s or q subunit results in a loss of function which can be restored by the addition of a myristoylation site. Because each of the –6qi4 and –6qs5 chimeric proteins of the prior art retained their native palmitoylation sites, there was no motivation in the art of record to add a myristoylation site to either of those two proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1800